Depressive Symptoms, Antidepressant Use, and the Incidence of Diabetes in the Black Women's Health Study

Varsha G. Vimalananda,[1] Julie R. Palmer,[2,3] Hanna Gerlovin,[2,4] Lauren A. Wise,[2,3] James L. Rosenzweig,[1] Lynn Rosenberg,[2,3] and Edward A. Ruiz-Narváez[2,3]

Diabetes Care 2014;37:2211–2217 | DOI: 10.2337/dc13-2642

OBJECTIVE

To assess the relationship of depressive symptoms and use of antidepressants with incident type 2 diabetes in prospective data from a large cohort of U.S. African American women.

RESEARCH DESIGN AND METHODS

The Black Women's Health Study (BWHS) is an ongoing prospective cohort study. We followed 35,898 women from 1999 through 2011 who were without a diagnosis of diabetes and who had completed the Center for Epidemiologic Studies Depression Scale (CES-D) in 1999. CES-D scores were categorized as <16, 16–22, 23–32, and ≥33, which reflected increasingly more depressive symptoms. We estimated incidence rate ratios (IRRs) and 95% CIs for incident diabetes using Cox proportional hazards models. The basic multivariable model included age, time period, family history of diabetes, and education. In further models, we controlled for lifestyle factors and BMI. We also assessed the association of antidepressant use with incident diabetes.

RESULTS

Over 12 years of follow-up, there were 3,372 incident diabetes cases. Relative to CES-D score <16, IRRs (95% CI) of diabetes for CES-D scores 16–22, 23–32, and ≥33 were 1.23 (1.12–1.35), 1.26 (1.12–1.41), and 1.45 (1.24–1.69), respectively, in the basic multivariate model. Multiple adjustment for lifestyle factors and BMI attenuated the IRRs to 1.11 (1.01–1.22), 1.08 (0.96–1.22), and 1.22 (1.04–1.43). The adjusted IRR for antidepressant use was 1.26 (1.11–1.43). Results were similar among obese women.

CONCLUSIONS

Both depressive symptoms and antidepressant use are associated with incident diabetes among African American women. These associations are mediated in part, but not entirely, through lifestyle factors and BMI.

The prevalence of type 2 diabetes among African American women is double that of white women and nearly 40% greater than that of African American men (1). Obesity is the strongest modifiable risk factor for diabetes (2) and has its highest prevalence among African American women (3), who are also less likely to exercise than people of other ethnic groups (4). Previous studies have also identified a moderately strong association between depression and incident diabetes (5–13), although whether this

[1]*Section of Endocrinology, Diabetes, and Nutrition, Boston University School of Medicine, Boston, MA*
[2]*Slone Epidemiology Center, Boston University, Boston, MA*
[3]*Department of Epidemiology, Boston University School of Public Health, Boston, MA*
[4]*Department of Biostatistics, Boston University School of Public Health, Boston, MA*

Corresponding author: Varsha G. Vimalananda, varshav@bu.edu.

Received 12 November 2013 and accepted 20 March 2014.

The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Minority Health and Health Disparities, the National Cancer Institute, the National Institutes of Health, or the American Heart Association.

relationship is mediated fully by obesity and lifestyle factors is not clear. Higher levels of inflammation (14) and dysregulation of the hypothalamic-pituitary-adrenal axis (15) are proposed to lie on the causal pathway between depression and incident diabetes and may explain some of the residual risk after multivariable adjustment that has been noted in prior work (7).

Despite the disproportionate burden of diabetes among African American women, prospective studies have shed little light on the relationship between depression and incident diabetes among African American women. Everson-Rose et al. (16) reported that in a 3-year multiethnic study, the adjusted association between depression and incident diabetes was strongest among African Americans. However, other studies conducted in the U.S. provide very few or no data on African Americans (5,6). Still other studies that include African Americans in larger numbers do not report adjusted estimates separately for African American women (7–9,11,13,17–19). In addition, although the risk of diabetes associated with antidepressants may be at least as high as that associated with depressive symptoms (13,20–22), we are unaware of investigations that explore the association between antidepressant use and incident diabetes among African American women.

In the current study, we assessed the relationship of depressive symptoms and antidepressant medication use to incident type 2 diabetes using prospective data from a large cohort of African American women. We also examined whether obesity and lifestyle factors are potential mediators of the relationship.

RESEARCH DESIGN AND METHODS

Study Population

We used data from the Black Women's Health Study (BWHS), an ongoing prospective cohort study of African American women from across the U.S. The BWHS was designed to investigate the determinants of health and disease in African American women. In 1995, women enrolled by responding to questionnaires mailed to subscribers of *Essence* magazine (a popular publication targeted to African American women), to members of several African American professional organizations, and to friends or relatives of early respondents. The final cohort included 59,000 women, aged 21–69 years at baseline in 1995 (23). The study protocol was approved by the institutional review boards of Boston University and Howard University, Washington, DC.

Participants completed a baseline questionnaire that included information on adult height, current weight, demographic characteristics, reproductive history, medical history, medication use, smoking, alcohol use, and diet. Every 2 years, mailed questionnaires collect updated information on lifestyle factors, other exposures, and medical problems, including diabetes. After eight cycles of follow-up to date, follow-up of the baseline cohort is 80%.

Questions about depressive symptoms were first asked in the 1999 questionnaire, and thus the present analyses are based on follow-up from 1999 through 2011. We excluded women with diabetes in 1999 (i.e., baseline in the present analysis) (n = 4,312), with diabetes diagnosed at age ≤30 years (n = 28), or with missing data on depressive symptoms at baseline (n = 16,564). We also excluded women with history of cancer (n = 1,424), myocardial infarction (n = 427), coronary artery bypass graft surgery (n = 146), and/or stroke (n = 430) at baseline. This resulted in a final analytic sample of 35,898 women.

Ascertainment of Depressive Symptoms and Antidepressant Use

Depressive symptoms were ascertained in 1999 (baseline in the present analyses) and 2005, using the Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is a 20-item self-report psychiatric instrument (24). It was designed by the National Institute of Mental Health Center for Epidemiologic Studies to identify symptoms of depression in community settings; it is not a diagnostic tool for clinical depression. The CES-D has been shown to be a reliable and valid tool for use in identifying the presence and severity of depressive symptoms in community settings and among African American women (24–26) and in the BWHS with a Cronbach α coefficient = 0.74, indicating high internal consistency (27). Respondents use a 4-point scale to indicate how often a symptom was experienced over the past week. Symptoms include those such as "I felt hopeful about the future", "I felt that people disliked me", and "I was bothered by things that don't usually bother me." Participants can select "Rarely or none of the time (0)", "Some or a little of the time (1)", "Occasionally or a moderate amount of the time (2)", or "Most or all of the time (3)." Total scores range from 0 to 60, with higher scores indicating more depressive symptoms. A cut point of ≥16 has traditionally been used in the literature to indicate the presence of depressive symptoms (24). At this level, the CES-D has a moderate to high sensitivity for major depression (60–100%) but a lower positive predictive value (24–48%) (28). In one community validation study, a cut point of 23 was used to distinguish "probable" from "possible" depression (29). In a study among pregnant African American women, a cut point of ≥33 was used (30). In concordance with previous work in the BWHS (31), we classified CES-D scores into four levels: <16, 16–22, 23–32, and ≥33. We used a score <16 to indicate few depressive symptoms, with each successively higher cut point indicating an increasing number of depressive symptoms.

Use of antidepressant medication was ascertained by the question "Do you take any of the following medications or vitamins at least 3 days a week?" Patients who marked yes for "Antidepressants (Prozac, Zoloft, Elavil, etc.)" were classified as using antidepressant medications. Questionnaires also included the open-ended question "Please list all other medications or supplements that you currently take at least 3 days a week." Participants who listed any antidepressant were classified as current users of antidepressant medication.

Ascertainment of Diabetes

The 1995 questionnaire and all biennial follow-up questionnaires asked participants if they had been diagnosed by a physician as having diabetes and when it was first diagnosed. Reported cases of diabetes were classified as incident if there was no report of a previous diagnosis. Participants were also asked in each questionnaire cycle whether they took injections or pills for diabetes; a positive response was also considered evidence of diabetes.

To assess the validity of self-reported diabetes, we had previously examined

the accuracy of self-reported diabetes among 227 randomly selected women who consented to release of medical records from their physicians and whose providers replied to the request. The diagnosis of type 2 diabetes was confirmed by the medical record in 218 (96%) of the 227 reported cases. Of the nine remaining participants, two had type 1 diabetes, one had metabolic syndrome, one had steroid-induced diabetes, two had gestational diabetes, and three did not have diabetes.

Covariates

Weight information was obtained from the baseline questionnaire (1999) and updated in biennial follow-up questionnaires. Adult height was reported in 1995. Current weight and 1995 height were used to calculate current BMI (kg/m^2). In a validation study of anthropometric measures conducted among 115 BWHS participants, Spearman correlations for self-reported versus technician-measured weight and height were 0.97 and 0.93, respectively (32). Data on vigorous physical activity, television watching, smoking, and alcohol drinking were obtained from the baseline questionnaire for the present analysis (1999) and updated in follow-up questionnaires. First-degree family history of diabetes was ascertained in 1995 and 1999. Educational attainment was asked in the 1995 and 2003 questionnaires. Information on energy intake was taken from 1995 and 2001 food frequency questionnaires (33,34).

Analysis

We compared age-adjusted baseline characteristics across the four CES-D score categories by computing means of continuous variables and proportions of categorical variables in each group.

Age- and time-stratified Cox proportional hazards regression was used to calculate incidence rate ratios (IRRs) and 95% CIs for the association of level of depressive symptoms and use of antidepressants with incident type 2 diabetes. Person-years of follow-up were calculated from baseline (1999) to the year of diagnosis of type 2 diabetes, loss to follow-up, death, or end of follow-up (2011), whichever came first. We used the Andersen-Gill approach to update time-varying exposures and covariates over follow-up. Depressive symptoms were updated in 2005; use of antidepressants and all the time-varying covariates were updated at every 2-year questionnaire cycle. To our basic multivariate model (adjusted for age, questionnaire cycle, healthcare utilization, first-degree family history of diabetes, and years of education), we added a group of lifestyle factors (vigorous physical activity [h/week], television watching [h/day], smoking [never use, past use, or current use], alcohol drinking [never use, past use, or current use], and dietary energy intake [kilocalories/day]) to assess whether symptoms of depression and use of antidepressants affect risk of diabetes through these behaviors. We further adjusted to determine whether BMI ($<$25, 25–29, 30–34, 35–39, and $\geq$40 kg/m^2) may lie on the causal pathway from depressive symptoms and use of antidepressants to incident diabetes. We restricted an analysis to obese women (BMI $\geq$30 kg/m^2), while adjusting for lifestyle factors, to test the hypothesis that symptoms of depression and use of antidepressants affect risk of type 2 diabetes through other pathways beyond lifestyle factors and BMI. For this analysis we adjusted for BMI as a continuous variable. We also assessed use of antidepressants within each category of CES-D score to assess their joint association with incident diabetes.

RESULTS

At baseline, of the 35,898 women included in the study, 71.5% scored $<$16 on the CES-D, 15.3% had CES-D score 16–23, 9.1% had CES-D score 23–33, and 4.1% had CES-D score $\geq$33 (Table 1). Baseline CES-D score was positively associated with BMI, caloric intake, antidepressant use, first-degree family history of diabetes, current smoking, current alcohol consumption, and television watching. CES-D score was inversely correlated with age, level of education, being married, vigorous exercise, and healthcare utilization.

Over 12 years with a total of 359,407 person-years of follow-up, there were 3,372 incident diabetes cases (Table 2). The numbers of cases per 1,000 person-years were 8.8 for CES-D $<$16, 10.4 for CESD-D 16–22, 10.8 for CES-D 23–32, and 13.0 for CES-D $\geq$33. According to use of antidepressants, the numbers of cases per 1,000 person-years were 9.0 for nonusers and 15.4 for users.

In the basic multivariate model, any level of CES-D score $\geq$16 was associated with a moderately increased diabetes risk (Table 2). Relative to CES-D scores $<$16, IRRs (95% CI) of incident diabetes for CES-D 16–22, 23–32, and $\geq$33 were 1.23 (1.12–1.35), 1.26 (1.12–1.41), and 1.45 (1.24–1.69), respectively. For all CES-D $\geq$16, we calculated an IRR of 1.27 (1.18–1.37). We observed attenuation of the IRRs after consecutive adjustment for lifestyle factors and BMI. The final multivariate model IRRs (95% CI) for diabetes were 1.11 (1.01–1.22) for CES-D 16–22, 1.08 (0.96–1.22) for

Table 1—Age-adjusted baseline (1999) characteristics by CES-D score categories*

	CES-D score categories			
Characteristic	$<$16	16–22	23–32	$\geq$33
Number of women	25,663	5,508	3,268	1,459
Mean age, years (SD)	42.1 (10.3)	39.9 (9.4)	39.2 (8.8)	38.6 (8.4)
Mean energy intake, kcal/day (SD)	1,420 (644)	1,481 (681)	1,521 (700)	1,598 (739)
Mean BMI, kg/m^2 (SD)	28.2 (6.2)	29.3 (6.5)	29.7 (6.8)	29.9 (6.8)
Education $\leq$12 years, %	14	18	21	23
Currently married, %	46	39	35	33
Antidepressant use, %	2	6	10	20
Family history of diabetes, %	36	38	39	39
Current smokers, %	12	17	19	24
Current alcohol drinkers, %	27	33	33	35
Vigorous exercise $\geq$5 h/week, %	10	7	7	6
Television watching $\geq$5 h/day, %	16	22	25	33
Use healthcare options,** %	96	95	95	92

*All of the characteristics vary significantly across CES-D group at the α = 0.05 level. **Based on having had a mammogram, Pap smear, or routine blood test in the course of a physical exam, over the past 2 years at baseline.

Table 2—IRR for diabetes according to CES-D score categories and use of antidepressant medication in the BWHS, 1999–2011

	CES-D score categories				Antidepressant use	
	<16	16–22	23–32	≥33	No	Yes
All BMI						
Cases/person-years	2,306/261,795	549/52,538	339/31,365	178/13,709	3,079/340,419	293/18,988
IRR						
Basic multivariate*	1.00 (reference)	1.23 (1.12–1.35)	1.26 (1.12–1.41)	1.45 (1.24–1.69)	1.00 (reference)	1.43 (1.26–1.62)
+Lifestyle factors†	1.00 (reference)	1.18 (1.07–1.30)	1.17 (1.04–1.32)	1.31 (1.12–1.53)	1.00 (reference)	1.35 (1.19–1.53)
+BMI	1.00 (reference)	1.11 (1.01–1.22)	1.08 (0.96–1.22)	1.22 (1.04–1.43)	1.00 (reference)	1.26 (1.11–1.43)
BMI ≥30 kg/m^2						
Cases/person-years	1,550/93,203	380/21,932	260/13,871	137/6,357	2,105/126,564	222/8,799
IRR‡	1.00 (reference)	1.06 (0.95–1.19)	1.10 (0.96–1.26)	1.24 (1.03–1.48)	1.00 (reference)	1.26 (1.09–1.46)

*Basic covariates: age, questionnaire cycle, healthcare utilization, family history of diabetes, and years of education. †Lifestyle factors: vigorous activity levels, daily hours of television watching, caloric intake, smoking, and alcohol consumption. ‡IRRs adjusted for all basic covariates + lifestyle factors + continuous BMI.

CES-D 23–33, and 1.22 (1.04–1.43) for CES-D ≥33; the comparable result for CES-D ≥16 was 1.12 (1.03–1.20). Similar results were obtained when restricting the analysis to obese women. Use of antidepressant medication was significantly associated with risk of diabetes in all the models (Table 2). In the final multivariate model, use of antidepressants was associated with a 26% higher risk of diabetes. We observed the same result among obese women: IRR 1.26 (95% CI 1.09–1.46).

Table 3 shows the results of the joint analysis of symptoms of depression and use of antidepressants, using as reference group women with CES-D score <16 who were not taking antidepressants. Those on antidepressants with CES-D scores ≥16 were at a significantly increased risk of incident diabetes in every model (Table 3). Symptoms of depression in the absence of antidepressant use were associated with diabetes in the basic multivariate model and after adjustment for lifestyle factors. However, in the full multivariate model, the association was observed only for the group of women with the highest number of depressive symptoms (CES-D ≥33). We observed similar results when restricting the analysis to obese women.

CONCLUSIONS

In this prospective study of a large cohort of African American women, we found a positive association between depressive symptoms and risk of incident type 2 diabetes; the association became stronger with increased number of depressive symptoms. Although the relationship was largely explained by demographic factors, lifestyle factors, and BMI, a positive association remained among those with the highest level of depressive symptoms regardless of antidepressant use. We also found an increased risk of diabetes associated with antidepressant use, and this association remained at every level of elevated depressive symptoms. It is noteworthy that both the highest levels of depressive symptoms and use of antidepressants were associated with an increased risk even among obese women, suggesting that both exposures may affect type 2 diabetes risk beyond any effect on obesity.

Although there are several studies that assessed the relationship of depression to incident diabetes, we found only one that reported data from African American women separately; it included 696 African American women and 41 cases over a follow-up period of 3 years (16). The study reported a rate ratio of 2.56 (95% CI 1.27–5.15) of diabetes for women with CES-D ≥16 relative to women CES-D <16, after adjusting for age, waist circumference, and physical activity (16). In our study, the comparable estimate was smaller, 1.12 (1.03–1.20). Our results were based on a larger sample (3,372 cases) and a longer follow-up period (12 years), and we adjusted our estimates for a wide variety of well-established contributors to diabetes risk, including family history, multiple lifestyle factors, and BMI. To our knowledge, ours is the largest prospective study of the association of depressive symptoms and diabetes among African American women, who bear a very large burden of illness due to diabetes.

Our finding that the relationship between CES-D scale score and diabetes is strongest for those with the highest level of depressive symptoms is consistent with other studies (7,8,11) and may reflect that those with the highest level of depressive symptoms on the CES-D scale are the most likely to have clinical depression with its common sequelae of decreased energy expenditure and obesity. Much of the increase in diabetes risk was explained by adjustment for these and other strong risk factors for diabetes, as has been reported in prior studies (6,7,16). However, antidepressant use appeared to represent additional increased risk that was persistent across CES-D scores and that was not explained by demographics, lifestyle, or BMI.

Most studies investigating the association between antidepressant use and incident diabetes have noted a positive association between the two (20,22,35–39). Among women with elevated depressive symptoms in the Women's Health Study, those who used antidepressants were at higher risk of incident diabetes compared with those who did not use them (13). In a recent meta-analysis, the use of antidepressant drugs was associated with an adjusted risk of diabetes of 1.68 (1.17–2.40), higher than our estimate of 1.26 (1.11–1.43), which was additionally adjusted for family history (21). Tricyclic antidepressants and selective serotonin reuptake inhibitors are both associated with weight gain (38,40). There is also some evidence that some, but not all, SSRIs induce cellular insulin resistance (41) and increased inflammatory markers (38). Other studies have found variation in the effects of different antidepressants on glucose homeostasis (42). More detailed examination of the

association of specific antidepressants with incident diabetes is an important avenue for future work.

Notably, we found that the associations of both higher-level depressive symptoms and antidepressants with incident diabetes persisted even among women with obesity. The group on antidepressants represents those whose mood symptoms were significant enough to have come to medical attention. It is plausible that the persistent increased risk of diabetes among African American women in these groups represents the action of more severe depression through unmeasured pathways known to be associated with both depression and diabetes, such as inflammatory (14) or neuroendocrine alterations (15).

Our study has several strengths, including its large size, the long-term and high rate of follow-up, and information on multiple important diabetes risk factors and potential confounders. There are also some limitations. We relied on self-reported measures of depressive symptoms, which introduce the possibility of exposure misclassification. The CES-D, however, is a well-validated tool that is commonly used to assess the presence of depressive symptoms in epidemiologic studies (7,16). Since symptoms were measured before the occurrence of diabetes, misclassification is likely to have been random and would have tended to attenuate associations in the extreme categories. We also relied on a self-reported diabetes diagnosis rather than clinical data. However, in a validation study, self-report was found to have high (96%) sensitivity for diabetes diagnosis. The prevalence of undiagnosed diabetes among African American women is ~4% (1), a degree of misclassification that is unlikely to have had a material effect on the estimates of risk that we calculated. In addition, we adjusted for healthcare utilization to account for any potential selection bias in the relationship between antidepressant use and diabetes. Although our results suggest that symptoms of depression and use of antidepressants affect risk of diabetes beyond behavior and BMI, we cannot rule out that the relationships we observed are due to residual confounding due to measurement error of these variables, or failure to control for other

Table 3—IRR for diabetes according to combined categories of CES-D score and use of antidepressant medication in the BWHS, 1999–2011

	CES-D score categories							
	<16		16–22		23–32		≥33	
On antidepressants	No	Yes	No	Yes	No	Yes	No	Yes
All BMI								
Cases/person-years	2,191/252,524	115/9,271	477/48,776	72/3,762	284/28,052	55/3,313	127/11,067	51/2,642
IRR								
Basic multivariate*	1.00 (reference)	1.30 (1.08–1.57)	1.19 (1.08–1.32)	2.07 (1.64–2.63)	1.25 (1.10–1.42)	1.80 (1.38–2.36)	1.45 (1.21–1.74)	2.01 (1.52–2.66)
+Lifestyle factors†	1.00 (reference)	1.20 (1.00–1.45)	1.14 (1.03–1.26)	1.89 (1.50–2.40)	1.16 (1.02–1.32)	1.61 (1.23–2.11)	1.30 (1.09–1.56)	1.74 (1.32–2.30)
+BMI	1.00 (reference)	1.13 (0.94–1.37)	1.08 (0.97–1.19)	1.64 (1.30–2.08)	1.08 (0.95–1.23)	1.33 (1.02–1.75)	1.20 (1.00–1.44)	1.58 (1.19–2.09)
BMI ≥30 kg/m^2								
Cases/person-years	1,466/89,243	84/3,960	323/20,101	57/1,831	220/12,158	40/1,713	96/5,062	41/1,295
IRR‡	1.00 (reference)	1.14 (0.92–1.43)	1.02 (0.91–1.15)	1.67 (1.28–2.18)	1.12 (0.97–1.30)	1.21 (0.88–1.66)	1.19 (0.97–1.47)	1.67 (1.22–2.29)

*Basic covariates: age, questionnaire cycle, healthcare utilization, family history of diabetes, and years of education. †Lifestyle factors: vigorous activity levels, daily hours of television watching, caloric intake, smoking, and alcohol consumption. ‡IRRs adjusted for all basic covariates + lifestyle factors + continuous BMI.

confounders. However, with regard to BMI, a previous validation study found that self-report of height and weight in the BWHS is highly accurate (32). In addition, the persistent association we find even among obese women suggests that at least for women with the highest number of depressive symptoms, there may be pathways independent from BMI. In addition, our group has previously reported significant associations of BMI (43) and behavior variables (44) with diabetes, suggesting that our covariate measures capture biologically relevant information.

In summary, we found a positive relationship between depressive symptoms and incident diabetes in a large population of African American women. Much, but not all, of this relationship was explained by lifestyle behaviors and obesity. In addition, we found an increase in risk in association with antidepressant use regardless of the severity of depressive symptoms. This may represent a direct effect of the medications. Alternately, there may be depression-associated biological factors among women with the severest symptoms, representing important paths for future studies.

Acknowledgments. The authors thank the BWHS participants for their continuing participation in this research effort.

Funding. This work was supported by National Institute on Minority Health and Health Disparities grant R01-MD-007015 and by National Cancer Institute grant R01-CA-058420. E.A.R.-N. is supported by grant 11SDG7390014 from the American Heart Association.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. V.G.V. and E.A.R.-N. analyzed the data and wrote the manuscript. J.R.P. and L.R. were responsible for the concept, design, and data collection in the BWHS, contributed to the discussion, and reviewed and edited the manuscript. H.G. conducted the statistical analysis. L.A.W. and J.L.R. contributed to the discussion and reviewed and edited the manuscript. E.A.R.-N. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. These results were previously presented at the 73rd Scientific Sessions of the American Diabetes Association, Chicago, IL, 21–25 June 2013.

References

1. Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health And Nutrition Examination Survey 1999-2002. Diabetes Care 2006;29:1263–1268
2. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature 2001;414:782–787
3. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. JAMA 2012;307:491–497
4. Crespo CJ, Keteyian SJ, Heath GW, Sempos CT. Leisure-time physical activity among US adults. Results from the Third National Health and Nutrition Examination Survey. Arch Intern Med 1996;156:93–98
5. Palinkas LA, Lee PP, Barrett-Connor E. A prospective study of type 2 diabetes and depressive symptoms in the elderly: the Rancho Bernardo Study. Diabet Med 2004;21:1185–1191
6. Arroyo C, Hu FB, Ryan LM, et al. Depressive symptoms and risk of type 2 diabetes in women. Diabetes Care 2004;27:129–133
7. Carnethon MR, Biggs ML, Barzilay JI, et al. Longitudinal association between depressive symptoms and incident type 2 diabetes mellitus in older adults: the cardiovascular health study. Arch Intern Med 2007;167:802–807
8. Mezuk B, Eaton WW, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: a meta-analysis. Diabetes Care 2008;31:2383–2390
9. Eaton WW, Armenian H, Gallo J, Pratt L, Ford DE. Depression and risk for onset of type II diabetes. A prospective population-based study. Diabetes Care 1996;19:1097–1102
10. Golden SH, Lee HB, Schreiner PJ, et al. Depression and type 2 diabetes mellitus: the multiethnic study of atherosclerosis. Psychosom Med 2007;69:529–536
11. Golden SH, Williams JE, Ford DE, et al.; Atherosclerosis Risk in Communities study. Depressive symptoms and the risk of type 2 diabetes: the Atherosclerosis Risk in Communities study. Diabetes Care 2004;27:429–435
12. Pan A, Lucas M, Sun Q, et al. Bidirectional association between depression and type 2 diabetes mellitus in women. Arch Intern Med 2010;170:1884–1891
13. Ma Y, Balasubramanian R, Pagoto SL, et al. Elevated depressive symptoms, antidepressant use, and diabetes in a large multiethnic national sample of postmenopausal women. Diabetes Care 2011;34:2390–2392
14. Schmidt MI, Duncan BB, Sharrett AR, et al. Markers of inflammation and prediction of diabetes mellitus in adults (Atherosclerosis Risk in Communities study): a cohort study. Lancet 1999;353:1649–1652
15. Golden SH. A review of the evidence for a neuroendocrine link between stress, depression and diabetes mellitus. Curr Diabetes Rev 2007;3:252–259
16. Everson-Rose SA, Meyer PM, Powell LH, et al. Depressive symptoms, insulin resistance, and risk of diabetes in women at midlife. Diabetes Care 2004;27:2856–2862
17. Everson-Rose SA, House JS, Mero RP. Depressive symptoms and mortality risk in a national sample: confounding effects of health status. Psychosom Med 2004;66:823–830
18. Knol MJ, Twisk JW, Beekman AT, Heine RJ, Snoek FJ, Pouwer F. Depression as a risk factor for the onset of type 2 diabetes mellitus. A meta-analysis. Diabetologia 2006;49:837–845
19. Ma Y, Hébert JR, Manson JE, et al. Determinants of racial/ethnic disparities in incidence of diabetes in postmenopausal women in the U.S.: The Women's Health Initiative 1993-2009. Diabetes Care 2012;35:2226–2234
20. Pan A, Sun Q, Okereke OI, et al. Use of antidepressant medication and risk of type 2 diabetes: results from three cohorts of US adults. Diabetologia 2012;55:63–72
21. Rotella F, Mannucci E. Depression as a risk factor for diabetes: a meta-analysis of longitudinal studies. J Clin Psychiatry 2013;74:31–37
22. Rubin RR, Ma Y, Peyrot M, et al.; Diabetes Prevention Program Research Group. Antidepressant medicine use and risk of developing diabetes during the diabetes prevention program and diabetes prevention program outcomes study. Diabetes Care 2010;33:2549–2551
23. Rosenberg L, Adams-Campbell L, Palmer JR. The Black Women's Health Study: a follow-up study for causes and preventions of illness. J Am Med Womens Assoc 1995;50:56–58
24. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401
25. Callahan CM, Wolinsky FD. The effect of gender and race on the measurement properties of the CES-D in older adults. Med Care 1994;32:341–356
26. Nguyen HT, Kitner-Triolo M, Evans MK, Zonderman AB. Factorial invariance of the CES-D in low socioeconomic status African Americans compared with a nationally representative sample. Psychiatry Res 2004;126:177–187
27. Williams CD, Taylor TR, Makambi K, et al. CES-D four-factor structure is confirmed, but not invariant, in a large cohort of African American women. Psychiatry Res 2007;150:173–180
28. Haringsma R, Engels GI, Beekman AT, Spinhoven P. The criterion validity of the Center for Epidemiological Studies Depression Scale (CES-D) in a sample of self-referred elders with depressive symptomatology. Int J Geriatr Psychiatry 2004;19:558–563
29. Husaini BA, Neff JA, Harrington JB, Hughes MD, Stone RH. Depression in rural communities: validating the CES-D scale. J Commun Pyschol 1980;8:20–27
30. Orr ST, James SA, Blackmore Prince C. Maternal prenatal depressive symptoms and spontaneous preterm births among African-American women in Baltimore, Maryland. Am J Epidemiol 2002;156:797–802
31. Phillips GS, Wise LA, Rich-Edwards JW, Stampfer MJ, Rosenberg L. Prepregnancy depressive symptoms and preterm birth in the Black Women's Health Study. Ann Epidemiol 2010;20:8–15
32. Carter-Nolan PL, Adams-Campbell LL, Makambi K, Lewis S, Palmer JR, Rosenberg L. Validation of physical activity instruments: Black Women's Health Study. Ethn Dis 2006;16:943–947
33. Block G, Hartman AM, Naughton D. A reduced dietary questionnaire: development and validation. Epidemiology 1990;1:58–64
34. Kumanyika SK, Mauger D, Mitchell DC, Phillips B, Smiciklas-Wright H, Palmer JR.

Relative validity of food frequency questionnaire nutrient estimates in the Black Women's Health Study. Ann Epidemiol 2003;13:111–118
35. Andersohn F, Schade R, Suissa S, Garbe E. Long-term use of antidepressants for depressive disorders and the risk of diabetes mellitus. Am J Psychiatry 2009;166:591–598
36. Kivimäki M, Hamer M, Batty GD, et al. Antidepressant medication use, weight gain, and risk of type 2 diabetes: a population-based study. Diabetes Care 2010;33:2611–2616
37. Knol MJ, Geerlings MI, Egberts AC, Gorter KJ, Grobbee DE, Heerdink ER. No increased incidence of diabetes in antidepressant users. Int Clin Psychopharmacol 2007;22:382–386
38. Sambamoorthi U, Ma Y, Findley PA, Rust G. Antidepressant use, depression, and new-onset diabetes among elderly Medicare beneficiaries. J Diabetes 2013;5:327–335
39. Bhattacharjee S, Bhattacharya R, Kelley GA, Sambamoorthi U. Antidepressant use and new-onset diabetes: a systematic review and meta-analysis. Diabetes Metab Res Rev 2013;29:273–284
40. Nihalani N, Schwartz TL, Siddiqui UA, Megna JL. Weight gain, obesity, and psychotropic prescribing. J Obes 2011;2011:893629
41. Levkovitz Y, Ben-Shushan G, Hershkovitz A, et al. Antidepressants induce cellular insulin resistance by activation of IRS-1 kinases. Mol Cell Neurosci 2007;36:305–312
42. McIntyre RS, Soczynska JK, Konarski JZ, Kennedy SH. The effect of antidepressants on glucose homeostasis and insulin sensitivity: synthesis and mechanisms. Expert Opin Drug Saf 2006;5:157–168
43. Krishnan S, Rosenberg L, Djoussé L, Cupples LA, Palmer JR. Overall and central obesity and risk of type 2 diabetes in U.S. black women. Obesity (Silver Spring) 2007;15:1860–1866
44. Krishnan S, Rosenberg L, Palmer JR. Physical activity and television watching in relation to risk of type 2 diabetes: the Black Women's Health Study. Am J Epidemiol 2009;169:428–434